Interval observers design for hybrid and biological systems

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Abstract

This work deals with interval observer design techniques. In the first part, the problem of interval observer design is studied for a class of linear hybrid systems. Several observers are proposed oriented on different conditions of positivity and stability for estimation error dynamics. Efficiency of the proposed approach is demonstrated by computer experiments for academic and bouncing ball systems. Note that interval observer design techniques for linear hybrid systems have been developed for the first time in the present work. The second part is devoted to the interval estimation of sequestred infected erythrocytes in plasmodium falciparum malaria patients. An advantage of the interval approaches in this case is that they give a bound of the errors at any time, which can be controlled in order to ensure the positivity of the state estimates of the system. Thus, interval estimation is very close to the reality in this case and has not been developed before the present work. An interval observer in order to estimate the sequestered parasite population is proposed in this report. Its efficiency is demonstrated by computer simulations.

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My inexpressible thanks to my fiancée Alexandrine. She always provides me an unconditional support and is an example of dedication and integrity to me.

To my newborn daughter Ariana Gracia

Contents

Introduction

There are many approaches dealing with the design techniques for state observers [1, 35, 17]. Frequently, these methods are based on (partial) linearity of the observed system, since analysis and design of stability and performance for linear systems are more developed. If it comes to take into account the presence of a disturbance or uncertain parameters, then synthesis of a conventional estimator (whose estimates are converging to the true values of the state) may be complicated [8, 1]. In such a case the problem of pointwise estimation can be substituted by the interval one, then using input-output measurements an observer has to estimate the set of admissible values (interval) for the state at each instant of time [19]. An advantage of interval observer is that it allows many types of uncertainties to be taken into account in the system. The interval observer design techniques have been developed for many types of models: continuous-time [31, 40], discrete-time [8, 32, 11, 33], time-delay [34, 9, 13] and algebraic-differential [10] ones.

Continuing this line, the problem of design of interval observers for linear hybrid systems [3, 18] is studied in this report. A hybrid system is a dynamic system that includes both continuous and discrete event dynamics [18]. The continuous dynamics are generally represented by differential equations and the discrete one by switching laws, which govern discontinuous jumps of continuous states [18]. The instants of these jumps can be time-dependent or state-dependent [3, 18]. Some kinds of other systems, like switched or impulsive ones for instance, can be presented in the hybrid framework. The main peculiarity of interval observation is that it is necessary to ensure positivity of the estimation error dynamics in addition to their stability. Since two types of dynamics (continuous and discrete) are present in the hybrid systems, then the conditions of positivity for these two cases (see [14] for examples) have to be combined, which leads to variety of the applicability conditions and design structures proposed in this work. Note that interval observer design techniques for linear hybrid systems is barely developed.

Furthermore the problem of interval estimation of sequestred infected erythrocytes in plasmodium falciparum malaria patients is discussed in this report. Malaria is a disease that causes at least one million deaths around the world each year, with ninety percent among African children. Plasmodium falciparum, the most dangerous type of malaria is caused by the most virulent species of the Plasmodium parasite [2]. In practice, only the peripheral infected erythrocytes (young parasites $y_1 + y_2 + ...y_k$, for some $k < n$), also called circulating, can be observed (seen on peripheral blood smears) and the other ones (sequestered: $y_{k+1}, ...y_n$) are hidden in some organs like brain and heart, and cannot be observed [2]. An interval observer in order to estimate the sequestered parasite population is proposed in this report. An advantage of the interval approaches in this case is that they give a bound of the errors at any time, which can be controlled in order to ensure the positivity of the parameters of the system. Thus, interval estimation is very close to the reality in this case and has not been developed before the present work.

The outline of the report is as follows. Some basic facts from the theories of interval estimation and hybrid systems are given in Chapter 1. In Chapter 2 the main results about hybrid linear systems are described and proven. In Section 2.4 these results are applied to some examples of hybrid systems, including a bouncing ball model. In Chapter 3 the main results about the interval estimation of sequestred infected erythrocytes in plasmodium falciparum malaria patients are described and proven. These results are applied using the measurements of the circulating parasitaemia $y_1 + y_2$ provided by [2] .

Chapter 1

Preliminaries

1.1 Introduction

How many fish can your tank safely hold? What fuel capacity should this train have if it is to carry passengers safely between Lille and Paris? Questions like these represent problems of estimation. These quantities must be estimated.

Exact answers are often impossible, difficult or expensive to obtain. However, approximate answers that are close to the exact answer may be obtained. Interval observers provide the set of admissible values (interval) for the state at each instant of time [19]. Some basic facts from the theories of interval estimation are given in this chapter. Then, two examples of interval estimation are given.

1.2 Notation

In this work, the real and integer numbers are denoted by $\mathbb{R}$ and $\mathbb{Z}$ respectively, $\mathbb{R}_+ = \{\tau \in \mathbb{R} : \tau \geq 0\}$ and $\mathbb{Z}_+ = \mathbb{Z} \cap \mathbb{R}_+$, $|x|$ is stated for the Euclidean norm of a vector $x \in \mathbb{R}^n$. For a measurable and locally essentially bounded input $u : \mathbb{R}_+ \to \mathbb{R}$ the symbol $||u||_{[t_0,t_1]}$ denotes its L_∞ norm:

$$||u||_{[t_0,t_1)} = ess \sup_{t\in[t_0,t_1)} |u(t)|,$$

if $t_1 = +\infty$ then we will simply write $||u||$. We will denote as $\mathcal{L}_\infty$ the set of all inputs u with the property $||u|| < \infty$. We will denote the sequence of integers $1, ..., n$ as $\overline{1, n}$. $E_{n\times m}$ denotes the matrix with all entries equal 1 (with dimensions $n \times m$). For a matrix $A \in \mathbb{R}^{n\times n}$ the vector of its eigenvalues is denoted as $\lambda(A)$. The relation $P \succ 0$ ($P \succeq 0$) for a symmetric matrix $P \in \mathbb{R}^{n\times n}$ means that it is positive (nonnegative) definite, the set of such $n \times n$ matrices will be denoted by $S^n_{\succ 0}$.

1.3 Interval analysis

For two vectors $x_1, x_2 \in \mathbb{R}^n$ or matrices $A_1, A_2 \in \mathbb{R}^{n\times n}$, the relations $x_1 \le x_2$ and $A_1 \le A_2$ are understood elementwise. Given a matrix $A \in \mathbb{R}^{m\times n}$, define $A^+ = \max\{0, A\}$, $A^- = A^+ - A$ (similarly for vectors) and denote the matrix of absolute values of all elements by $|A| = A^+ + A^-$.

Lemma 1. [7] *Let $x \in \mathbb{R}^n$ be a vector variable, $\underline{x} \le x \le \overline{x}$ for some $\underline{x}, \overline{x} \in \mathbb{R}^n$, and $A \in \mathbb{R}^{m\times n}$ be a constant matrix, then*

$$A^+\underline{x} - A^-\overline{x} \le Ax \le A^+\overline{x} - A^-\underline{x}. \tag{1.1}$$

1.4 Nonnegative continuous-time linear systems

A matrix $A \in \mathbb{R}^{n\times n}$ is called Hurwitz if all its eigenvalues have negative real parts, it is called Metzler if all its elements outside the main diagonal are nonnegative, *i.e.* $A_{i,j} \ge 0$ for $1 \le i \ne j \le n$. Any solution of the linear system

$$\begin{aligned} \dot{x} &= Ax + B\omega(t),\ \omega : \mathbb{R}_+ \to \mathbb{R}^q_+, \\ y &= Cx + D\omega(t), \end{aligned} \tag{1.2}$$

with $x \in \mathbb{R}^n$, $y \in \mathbb{R}^p$ and a Metzler matrix $A \in \mathbb{R}^{n\times n}$, is elementwise nonnegative for all $t \ge 0$ provided that $x(0) \ge 0$ and $B \in \mathbb{R}^{n\times q}_+$ [16, 45]. The output solution $y(t)$ is nonnegative if $C \in \mathbb{R}^{p\times n}_+$ and $D \in \mathbb{R}^{p\times q}_+$. Such dynamical systems are called cooperative (monotone) or nonnegative if only initial conditions in $\mathbb{R}_+^n$ are considered [16, 45].

For a Metzler matrix $A \in \mathbb{R}^{n\times n}$ its stability can be checked verifying a Linear Programming (LP) problem

$$A^{\mathrm{T}}\lambda < 0$$

for some $\lambda \in \mathbb{R}_+^n \setminus \{0\}$.

1.5 Nonnegative discrete-time linear systems

A matrix $A \in \mathbb{R}^{n\times n}$ is called Schur stable if all its eigenvalues have absolute value less than one, it is called nonnegative if all its elements are nonnegative (*i.e.* $A \geq 0$). Any solution of the system

$$x_{t+1} = Ax_t + B\omega_t,\ \omega : \mathbb{Z}_+ \to \mathbb{R}_+^m,\ t \in \mathbb{Z}_+$$

with $x_t \in \mathbb{R}^n$ and nonnegative matrices $A \in \mathbb{R}_+^{n\times n}$ and $B \in \mathbb{R}_+^{n\times m}$, is elementwise nonnegative for all $t \in \mathbb{Z}_+$ provided that $x(0) \geq 0$ [23]. Such a system is called cooperative (monotone) or nonnegative [23].

Lemma 2. [16] *A matrix $A \in \mathbb{R}_+^{n\times n}$ is Schur stable iff there exists a diagonal matrix $P \in S_{\succ 0}^n$ such that $A^T PA - P \prec 0$.*

1.6 A non-homogeneous sliding mode differentiator

Let $\tilde{y}(t) = y(t) + \nu(t)$ be a measured signal, where $y : \mathbb{R}_+ \to \mathbb{R}$ is a signal to be differentiated and $\nu \in \mathcal{L}_\infty$ is a bounded measurement noise, then a differentiator can be proposed [15]:

$$
\begin{aligned}
\dot{x}_1 &= -\alpha\sqrt{|x_1 - \tilde{y}(t)|}\,\mathbf{sign}(x_1 - \tilde{y}(t)) + x_2, \\
\dot{x}_2 &= -\varrho\,\mathbf{sign}(x_1 - \tilde{y}(t)) - \chi\,\mathbf{sign}(x_2) - x_2, \\
& x_1(0) = \tilde{y}(0),\ x_2(0) = 0,
\end{aligned} \tag{1.3}
$$

where $x_1, x_2 \in \mathbb{R}$ are the state variables of the system (1.3), α, ϱ and χ are the tuning parameters with $\alpha > 0$ and $\varrho > \chi \geq 0$. The variable $x_1(t)$ serves as an estimate of the function $y(t)$ and $x_2(t)$ is an estimate of $\dot{y}(t)$, *i.e.* it provides the derivative estimate. Therefore, the system (1.3) has $\tilde{y}(t)$ as the input and $\hat{\dot{y}}(t) = x_2(t)$ as the output.

Lemma 3. [15] *Let $\dot{y}, \ddot{y}, \nu \in \mathcal{L}_\infty$, then there exist $\alpha > 0$ and $\varrho > \chi \geq 0$ such that $x_1, x_2 \in \mathcal{L}_\infty$ and there exist $T_0 > 0$, $c_1 > 0$ and $c_2 > 0$:*

$$|x_2(t) - \dot{y}(t)| \leq \sqrt{c_1||\nu||_\infty + \sqrt{c_2||\nu||_\infty}} \quad \forall t \geq T_0.$$

Estimates on $T_0 > 0$, $c_1 > 0$, $c_2 > 0$ and guidelines for tuning α, ϱ, χ can also be found in [15].

1.7 Example of interval observer [7]

Consider an LTI continuous-time system:

$$
\begin{aligned}
\dot{x}(t) &= Ax(t) + b(t), \\
y(t) &= Cx(t) + v(t),
\end{aligned} \tag{1.4}
$$

where $x(t) \in \mathbb{R}^n$ is the state; $y(t) \in \mathbb{R}^p$ is the output signal available for measurements; $b : \mathbb{R}_+ \to \mathbb{R}^n$, $b \in \mathcal{L}_\infty$ is the input; $v : \mathbb{R}_+ \to \mathbb{R}^p$, $v \in \mathcal{L}_\infty$ is the measurement noise; A and C are real matrices of the corresponding dimensions.

Assume that the state $x(t)$ is bounded, *i.e.* $x \in \mathcal{L}_\infty$. Assume that there exist a matrix $L \in \mathbb{R}^{n\times p}$, such that the matrix $(A - LC)$ is Hurwitz and Metzler. Let two functions $\underline{b}$, $\overline{b} : \mathbb{R}_+ \to \mathbb{R}^n$, $\underline{b}$, $\overline{b} \in \mathcal{L}_\infty$ are given such that $\underline{b}(t) \leq b(t) \leq \overline{b}(t) \quad \forall t \in \mathbb{R}_+$. Let also two functions $\underline{d}$, $\overline{d} : \mathbb{R}_+ \to \mathbb{R}^n$,

$\underline{d}, \overline{d} \in \mathcal{L}_\infty$ are given such that $\underline{d}(t) \leq d(t) \leq \bar{d}(t) \quad \forall t \in \mathbb{R}_+$. Assume that the constant $0 \leq V \leq +\infty$ is given such that $||v|| < V$.

Under the introduced assumptions an interval observer equations for (1.4) take the form:

$$\begin{aligned} \dot{\underline{x}}(t) &= (A - LC)\underline{x}(t) + Ly(t) + \underline{b}(t) - \overline{L}V, \\ \dot{\overline{x}}(t) &= (A - LC)\overline{x}(t) + Ly(t) + \bar{b}(t) + \overline{L}V, \end{aligned} \tag{1.5}$$

where $\underline{x}(t) \in \mathbb{R}^n$ and $\overline{x}(t) \in \mathbb{R}^n$ are respectively the lower and the upper interval estimates for the state $x(t)$, $\overline{L} = |L|E_{p\times 1}$ and $\overline{M} = |M|E_{p\times 1}$. Then for all $t \in \mathbb{R}_+$ the estimates $\underline{x}(t)$ and $\overline{x}(t)$ given by (1.5) are bounded and $\underline{x}(t) \leq x(t) \leq \bar{x}(t)$ provided that $\underline{x}(0) \leq x(0) \leq \bar{x}(0)$.

1.8 Example of application of interval estimation

Let's apply the interval observer of the previous section to an example of a biochemical oscillator based on negative feedback. It is described by Brian C. Goodwin's equations [30]:

$$\begin{aligned} \dot{x_1} &= \frac{a}{1 + x_2^\rho} - \alpha x_1 + d(t), \\ \dot{x_2} &= c x_1 - \alpha x_2, \\ y &= x_2, \end{aligned}$$

where we take $\alpha = 0.1,\ c = 1,\ a = 0.2\sin(t) + 1,\ \rho = \sin(t) + 6,\ d(t) = 0.001\sin(t),\ x(t) = \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} \in \mathbb{R}^2$ is the state and $y(t) \in \mathbb{R}$ is the output signal available for measurements.

This system can be identified as a system (1.4) with $v(t) = 0$ where the matrices A and C are defined as follows:

$$A = \begin{bmatrix} -\alpha & 0 \\ c_1 & -\alpha \end{bmatrix},\ C = \begin{bmatrix} 0 & 1 \end{bmatrix}.$$

The signal $b(t)$ is:

$$b(t) = \begin{bmatrix} \frac{a}{1+x_2^{\rho}} + d(t) \\ 0 \end{bmatrix} = \begin{bmatrix} \frac{a}{1+y^{\rho}} + d(t) \\ 0 \end{bmatrix}.$$

Thus when $y \geq 1$,

$$\begin{aligned} \underline{d}(t) &= -0.001, \\ \overline{d}(t) &= 0.001, \\ \underline{a} &= -0.2, \\ \overline{a} &= 0.2, \\ \underline{\rho} &= 5, \\ \overline{\rho} &= 7, \\ \underline{b}(t) &= \begin{bmatrix} -\delta + \frac{\underline{a}}{1+y^{\overline{\rho}}} \\ 0 \end{bmatrix}, \\ \overline{b}(t) &= \begin{bmatrix} \delta + \frac{\bar{a}}{1+y^{\underline{\rho}}} \\ 0 \end{bmatrix}. \end{aligned}$$

When $y \leq 1$,

$$\begin{aligned} \underline{d}(t) &= -0.001, \\ \overline{d}(t) &= 0.001, \\ \underline{a} &= -0.2, \\ \overline{a} &= 0.2, \\ \underline{\rho} &= 5, \\ \overline{\rho} &= 7, \\ \overline{b}(t) &= \begin{bmatrix} -\delta + \frac{\underline{a}}{1+y^{\underline{\rho}}} \\ 0 \end{bmatrix}, \\ \overline{b}(t) &= \begin{bmatrix} \delta + \frac{\bar{a}}{1+y^{\overline{\rho}}} \\ 0 \end{bmatrix}. \end{aligned}$$

Assume that $||x|| < +\infty$. For $L = \begin{bmatrix} 0 & -5 \end{bmatrix}^{\mathrm{T}}$, the matrix $A - LC =$

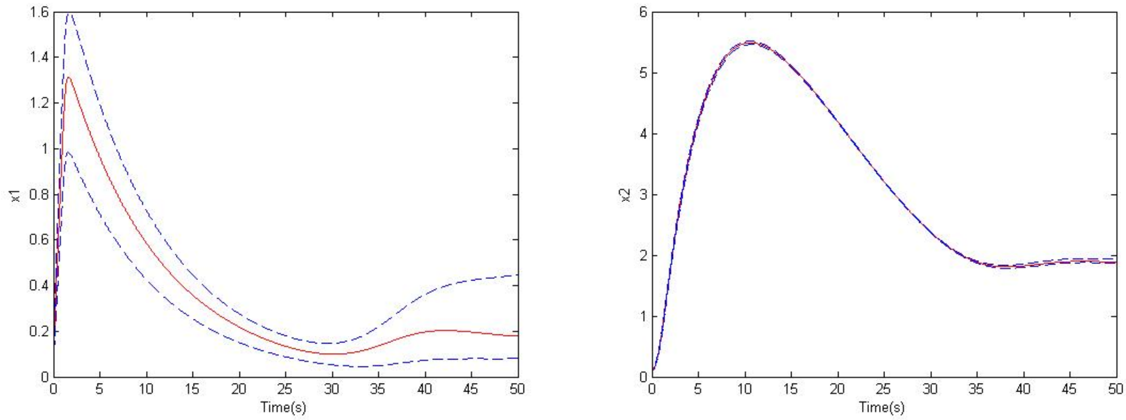

Figure 1.1: Results of the simulation for the biochemical oscillator system

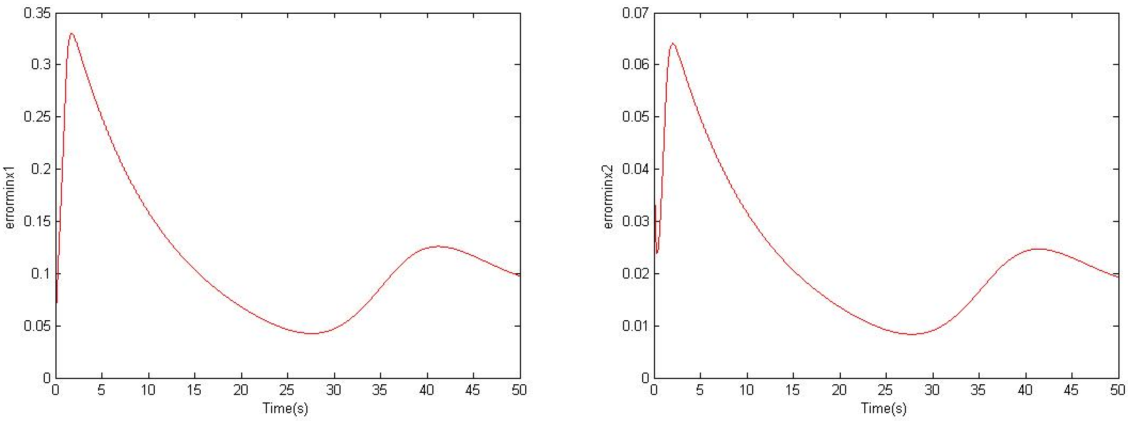

Figure 1.2: Evolution of $\underline{e}$(t) for the biochemical oscillator system

$\begin{bmatrix} -0.1 & 0 \\ 1 & -5.1 \end{bmatrix}$ is Hurwitz and Metzler. Therefore all conditions are satisfied and the interval observer (1.5) solves the problem of interval state estimation. The results of simulation are shown in Fig 1.4, where the solid lines represent the states x_k, $k = 1, 2$ and the dash lines are used for the interval estimates $\underline{x_k}$ and $\overline{x_k}$.

The errors $\underline{e}(t) = x(t) - \underline{x}(t)$, $\overline{e}(t) = \overline{x}(t) - x(t)$ are shown respectively in Fig 1.2 and in Fig 1.3.

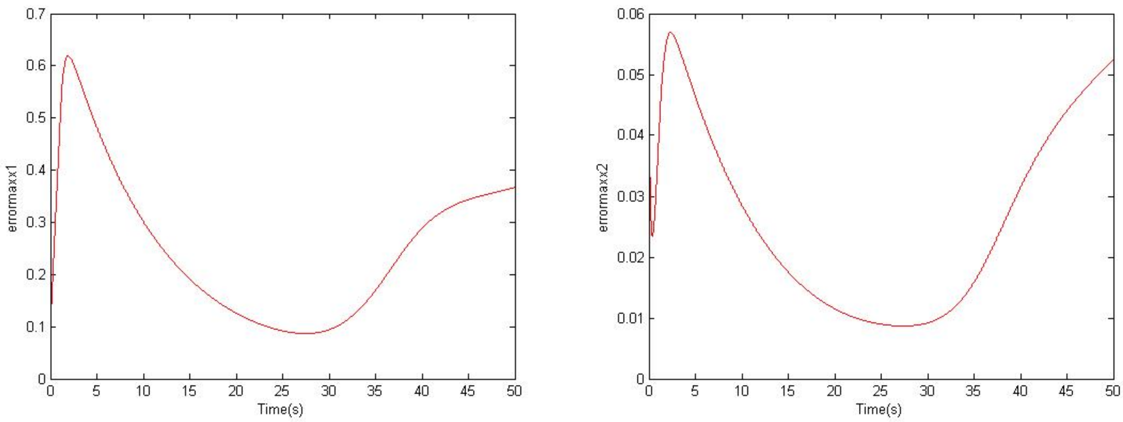

Figure 1.3: Evolution of $\overline{e}$(t) for the biochemical oscillator system

1.9 Another example of interval observer [7]

Let all the assumptions of the interval observer (1.5) be satisfied except the fact that there doesn't exist a matrix $L \in \mathbb{R}^{n\times p}$, such that the matrix $(A - LC)$ is Metzler. There exist a Metzler matrix R such that $\lambda(A - LC) = \lambda(R)$, the pairs $(A - LC, e_1)$, (R, e_2) are observable for some $e_j \in \mathbb{R}^{1\times n}$ with $j = \overline{1,2}$. Then for all $t \in \mathbb{R}_+$ the estimates $\underline{x}(t)$ and $\overline{x}(t)$ are bounded and $\underline{x}(t) \leq x(t) \leq \bar{x}(t)$ provided that $\underline{x}(0) \leq x(0) \leq \bar{x}(0)$, where

$$\begin{aligned}
\underline{x}(t) &= S^{+}\underline{z}(t) - S^{-}\overline{z}(t), \\
\overline{x}(t) &= S^{+}\overline{z}(t) - S^{-}\underline{z}(t), \\
\dot{\underline{z}}(t) &= R\underline{z}(t) + Fy(t) - \overline{F}V + (S^{-1})^{+}\underline{b}(t) - (S^{-1})^{-}\overline{b}(t), \qquad (1.6)\\
\dot{\overline{z}}(t) &= R\overline{z}(t) + Fy(t) + \overline{F}V + (S^{-1})^{+}\overline{b}(t) - (S^{-1})^{-}\underline{b}(t), \\
\underline{z}(0) &= (S^{-1})^{+}\underline{x}(0) - (S^{-1})^{-}\overline{x}(0), \\
\overline{z}(0) &= (S^{-1})^{+}\overline{x}(0) - (S^{-1})^{-}x(0),
\end{aligned}$$

where $S = O_R O_{A-LC}^{-1}$(O_{A-LC} and O_R are the observability matrices of the pairs $(A - LC, e_1)$, (R, e_2) respectively), $F = S^{-1}L$ and $\overline{F} = (F^{+} + F^{-})E_{p\times 1}$.

1.10 Example of application of interval estimation

Let's apply the interval observer of the previous section to an example of a Rössler attractor. It is described by a system of three non-linear ordinary differential equations originally studied by Otto Rössler [42, 43, 39, 26, 27, 29, 44]:

$$\begin{aligned} \dot{x_1} &= -x_2 - x_3 + d_1(t), \\ \dot{x_2} &= x_1 + ax_2 + d_2(t), \\ \dot{x_3} &= b + x_3(x_1 - c) + d_3(t), \\ y &= Cx + v(t), \end{aligned} \tag{1.7}$$

where $a = 0.2,\ b = 0.2,\ c = 5.7,\ d_1(t) = d_2(t) = d_3(t) = 0.05\sin(t),\ x(t) = \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} \in \mathbb{R}^3$ is the state, $v(t) = \begin{bmatrix} 0.05\sin(t) \\ 0.05\sin(t) \end{bmatrix}$, $C = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix}$ and $y(t) \in \mathbb{R}$ is the output signal available for measurements.

This system can be identified as a system (1.4) where the matrices A and C are defined as follows:

$$A = \begin{bmatrix} 0 & -1 & -1 \\ 1 & a & 0 \\ 0 & 0 & -c \end{bmatrix}.$$

The signal $b(t)$ is:

$$b(t) = \begin{bmatrix} d_1(t) \\ d_2(t) \\ d_3(t) + b + x_1x_3 \end{bmatrix}.$$

Thus,

$$V = \begin{bmatrix} V_1 \\ V_2 \end{bmatrix} = \begin{bmatrix} 0.05 \\ 0.05 \end{bmatrix},$$

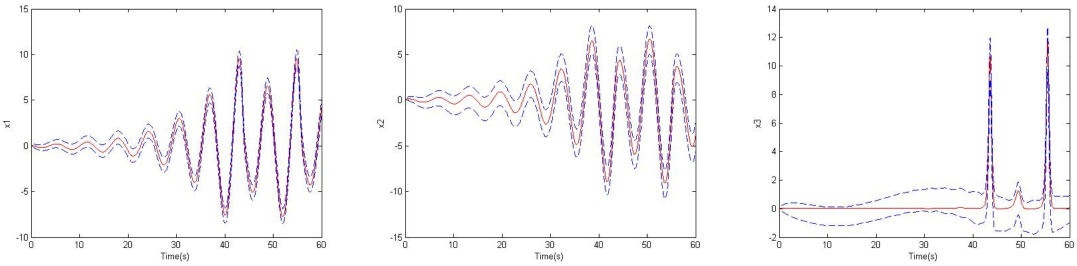

Figure 1.4: Results of the simulation for the Rossler attractor

and

$$\underline{b}(t) = \begin{bmatrix} -0.05 \\ -0.05 \\ -0.05 + b + y_1 y_2 - V_1 V_2 - V_1|y_2| - V_2|y_1| \end{bmatrix},$$
$$\overline{b}(t) = \begin{bmatrix} 0.05 \\ 0.05 \\ 0.05 + b + y_1 y_2 + V_1 V_2 + V_1|y_2| + V_2|y_1| \end{bmatrix}.$$

Assume that $||x|| < +\infty$. Therefore all conditions are satisfied. Finally, the matrices

$$R = \begin{bmatrix} -2 & 0 & 0 \\ 0 & -0.1 & 0 \\ 0 & 0 & -0.5 \end{bmatrix}$$
$$S = \begin{bmatrix} -0.9578 & 0.4138 & 0 \\ 0.2873 & -0.9104 & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

satisfy all conditions of the interval observer (1.6) and this one solves the problem of interval state estimation for the Rössler attractor. The results of simulation are shown in Fig 1.4, where the solid lines represent the states x_k, $k = 1, 3$ and the dash lines are used for the interval estimates $\underline{x_k}$ and $\overline{x_k}$.

The errors $\underline{e}(t) = x(t) - \underline{x}(t)$, $\overline{e}(t) = \overline{x}(t) - x(t)$ are shown respectively in Fig 1.5 and in Fig 1.6.

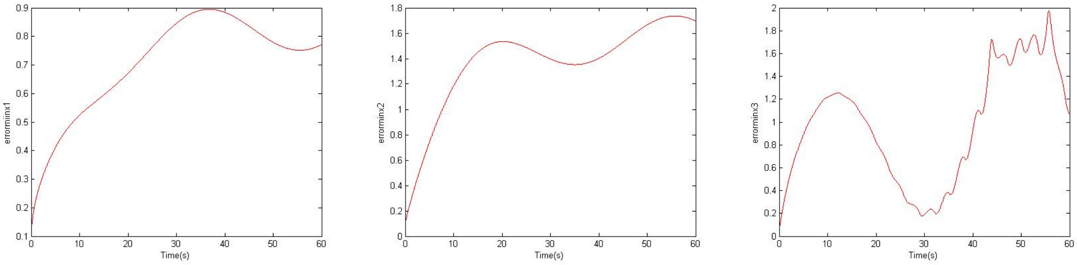

Figure 1.5: Evolution of $\underline{e}(t)$ for the Rossler attractor

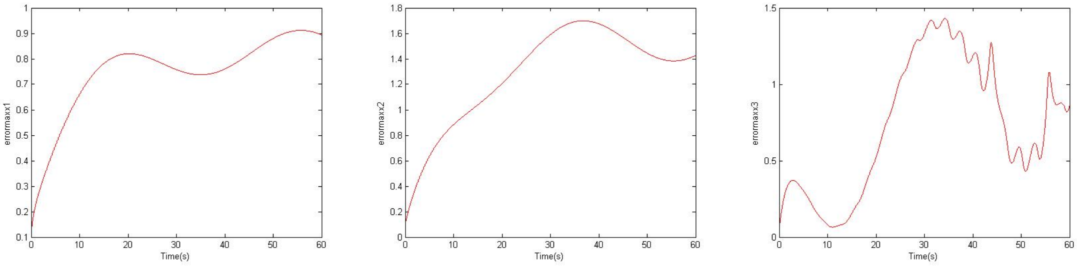

Figure 1.6: Evolution of $\overline{e}(t)$ for the Rossler attractor

1.11 Conclusion

In this part of the report, basic facts from the theories of interval estimation are given. These tools will be heavily used in the next chapter treating the interval estimation of hybrid systems.

Chapter 2

Interval Observers for Hybrid Linear Systems

2.1 Introduction

In this chapter, we focus in particular on the problem of design of interval observers for linear hybrid systems [3, 18]. A hybrid system is a dynamic system that includes both continuous and discrete event dynamics [18]. The main results are described and proven. In Section 2.4 these results are applied to some examples of hybrid systems, including a bouncing ball model.

2.2 Stability of hybrid systems under ranged dwell-time

Consider a hybrid (impulsive) linear system

$$\begin{aligned} \dot{x}(t) &= Ax(t) + b(t) \quad \forall t \in [t_i, t_{i+1}),\ i \in \mathbb{Z}_+, \\ x(t_{i+1}) &= Gx(t_{i+1}^-) + d(t_{i+1}) \quad \forall i \geq 1, \end{aligned} \tag{2.1}$$

where $x(t) \in \mathbb{R}^n$ is the state vector and $x(t_{i+1}^-)$ is the left-sided limit of $x(t)$ for $t \to t_{i+1}$; $A, G \in \mathbb{R}^{n\times n}$; $b : \mathbb{R}_+ \to \mathbb{R}^n$, $b \in \mathcal{L}_\infty$ is the input $\forall t \in [t_i, t_{i+1})$; $d : \mathbb{R}_+ \to \mathbb{R}^n$, $d \in \mathcal{L}_\infty$ is the input at time instants

$t_{i+1}\,\forall i \geq 1$. The sequence of impulse events t_i with $i \in \mathbb{Z}_+$ is assumed to be positive increment, *i.e.* $T_i = t_{i+1} - t_i > 0$ and $t_0 = 0$.

Theorem 1. [4] *Consider system (2.1) with* $||b|| = ||d|| = 0$ *and a ranged dwell-time* $T_i \in [T_{\min}, T_{\max}]$ *for all* $i \in \mathbb{Z}_+$, *where* $0 \leq T_{\min} \leq T_{\max} < +\infty$ *are given constants. Then it is asymptotically stable provided that there exists a matrix* $P \in S^n_{\succ 0}$ *such that for all* $\theta \in [T_{\min}, T_{\max}]$

$$G^T e^{A^T\theta} P e^{A\theta} G - P \prec 0. \tag{2.2}$$

The proof of the above theorem is based on the fact that in this case $V(x) = x^{\mathrm{T}} P x$ is a Lyapunov function for (2.1) at discrete instants of time t_i. Following [22, 6], robustness with respect to the inputs b and d can be proven (see the definition of the input-to-state stability (ISS) given in those works):

Corollary 1. *Consider system (2.1) with a ranged dwell-time* $T_i \in [T_{\min}, T_{\max}]$ *for all* $i \in \mathbb{Z}_+$, *where* $0 \leq T_{\min} \leq T_{\max} < +\infty$ *are given constants. Then it is ISS provided that there exists a matrix* $P \in S^n_{\succ 0}$ *such that for all* $\theta \in [T_{\min}, T_{\max}]$ *the LMI (2.2) is satisfied.*

This result implies that (2.1) has bounded solutions for any bounded inputs b and d if the LMI (2.2) is valid.

2.3 Main results

Consider hybrid system (2.1) with the output signal $y(t) \in \mathbb{R}^p$ available for measurements:

$$y(t) \quad = \quad Cx(t) + v(t),$$

where $v \in \mathcal{L}_\infty$ is the measurement noise; $C \in \mathbb{R}^{p \times n}$. We will need the following assumptions for (2.1):

Assumption 1. *The state* $x(t)$ *is bounded,* i.e. $x \in \mathcal{L}_\infty$, *and* $T_i = t_{i+1} - t_i \in [T_{\min}, T_{\max}]$ *for all* $i \in \mathbb{Z}_+$, *where* $0 \leq T_{\min} \leq T_{\max} < +\infty$ *are given constants.*

Assumption 2. *There exist matrices* $L \in \mathbb{R}^{n\times p}$, $M \in \mathbb{R}^{n\times p}$, $P \in S^n_{\succ 0}$ *such that:*

i) the LMI

$$(G - MC)^T e^{(A-LC)^T\theta} P e^{(A-LC)\theta}(G - MC) - P \prec 0 \tag{2.3}$$

holds for all $\theta \in [T_{\min}, T_{\max}]$;

ii) the matrix $(A - LC)$ *is Metzler;*

iii) the matrix $(G - MC)$ *is nonnegative.*

When the assumption 2.i holds, the quadratic form $V(x) = x^{\mathrm{T}}Px$ is a discrete-time Lyapunov function for the LTI discrete-time system $z_{i+1} = e^{(A-LC)\theta}(G - MC)z_i$ for all $\theta \in [T_{\min}, T_{\max}]$ and $i \in \mathbb{Z}_+$ by Theorem 1.

Assumption 3. *Let*

i) two functions $\underline{b}$, $\bar{b} : \mathbb{R}_+ \to \mathbb{R}^n$, $\underline{b}$, $\bar{b} \in \mathcal{L}_\infty$ *are given such that*

$$\underline{b}(t) \le b(t) \le \bar{b}(t) \quad \forall t \in \mathbb{R}_+;$$

ii) two functions $\underline{d}$, $\bar{d} : \mathbb{R}_+ \to \mathbb{R}^n$, $\underline{d}, \bar{d} \in \mathcal{L}_\infty$ *are given such that*

$$\underline{d}(t) \le d(t) \le \bar{d}(t) \quad \forall t \in \mathbb{R}_+;$$

iii) the constant $0 \le V \le +\infty$ *is given such that* $||v|| < V$.

Under the introduced assumptions an interval observer equations for (2.1) take the form $\forall i \in \mathbb{Z}_+$:

$$\begin{aligned}
\dot{\underline{x}}(t) &= (A - LC)\underline{x}(t) + Ly(t) + \underline{b}(t) \\
&\quad -\overline{L}V \;\forall t \in [t_i, t_{i+1}), \\
\underline{x}(t_{i+1}) &= (G - MC)\underline{x}(t^-_{i+1}) + My(t_{i+1}) \\
&\quad +\underline{d}(t_{i+1}) - \overline{M}V, \\
\dot{\overline{x}}(t) &= (A - LC)\overline{x}(t) + Ly(t) + \bar{b}(t) \\
&\quad +\overline{L}V \;\forall t \in [t_i, t_{i+1}), \\
\overline{x}(t_{i+1}) &= (G - MC)\overline{x}(t^-_{i+1}) + My(t_{i+1}) \\
&\quad +\bar{d}(t_{i+1}) + \overline{M}V,
\end{aligned} \tag{2.4}$$

where $\underline{x}(t) \in \mathbb{R}^n$ and $\overline{x}(t) \in \mathbb{R}^n$ are respectively the lower and the upper interval estimates for the state $x(t)$, $\overline{L} = |L|E_{p\times 1}$ and $\overline{M} = |M|E_{p\times 1}$.

Theorem 2. *Let assumptions 1–3 be satisfied. Then for all $t \in \mathbb{R}_+$ the estimates $\underline{x}(t)$ and $\overline{x}(t)$ given by (2.4) are bounded and*

$$\underline{x}(t) \leq x(t) \leq \bar{x}(t) \tag{2.5}$$

provided that $\underline{x}(0) \leq x(0) \leq \bar{x}(0)$.

Proof. The equation (2.1) can be rewritten as follows:

$$\begin{aligned}
\dot{x}(t) &= (A - LC)x(t) + L[y(t) - v(t)] \\
&\quad + b(t)\ \forall t \in [t_i, t_{i+1}), \\
x(t_{i+1}) &= (G - MC)x(t_{i+1}^-) + M[y(t_{i+1}) - v(t_{i+1})] \\
&\quad + d(t_{i+1}).
\end{aligned}$$

Then the dynamics of the errors $\underline{e}(t) = x(t) - \underline{x}(t)$, $\overline{e}(t) = \overline{x}(t) - x(t)$ obey the equations for all $i \in \mathbb{Z}_+$:

$$\begin{aligned}
\dot{\underline{e}}(t) &= (A - LC)\underline{e}(t) + \underline{g_1}(t)\ \forall t \in [t_i, t_{i+1}), \\
\underline{e}(t_{i+1}) &= (G - MC)\underline{e}(t_{i+1}^-) + \underline{g_2}(t_{i+1}), \\
\dot{\overline{e}}(t) &= (A - LC)\overline{e}(t) + \overline{g_1}(t)\ \forall t \in [t_i, t_{i+1}), \\
\overline{e}(t_{i+1}) &= (G - MC)\overline{e}(t_{i+1}^-) + \overline{g_2}(t_{i+1}),
\end{aligned} \tag{2.6}$$

where

$$\begin{aligned}
\underline{g_1}(t) &= [\overline{L}V - Lv(t)] + [b(t) - \underline{b}(t)], \\
\underline{g_2}(t_{i+1}) &= [\overline{M}V - Mv(t_{i+1})] + [d(t_{i+1}) - \underline{d}(t_{i+1})], \\
\overline{g_1}(t) &= [\overline{L}V + Lv(t)] + [\overline{b}(t) - b(t)], \\
\overline{g_2}(t_{i+1}) &= [\overline{M}V + Mv(t_{i+1})] + [\overline{d}(t_{i+1}) - d(t_{i+1})].
\end{aligned}$$

According to Assumption 3 we have $\underline{g_1}, \overline{g_1}, \underline{g_2}, \overline{g_2} \in \mathcal{L}_\infty$; $\underline{g_1}(t) \geq 0$, $\overline{g_1}(t) \geq 0$ $\forall t \in [t_i; t_{i+1})$ and $\underline{g_2}(t_{i+1}) \geq 0$, $\overline{g_2}(t_{i+1}) \geq 0$ $\forall i \geq 1$. When Assumption 2.i holds, the system (2.6) with ranged dwell-time $T_i \in [T_{\min}, T_{\max}]$

(Assumption 1) is asymptotically stable for $\underline{g_k} = \overline{g_k} = 0$, $k = 1, 2$ and it has bounded state variables for bounded $\underline{g_k}, \overline{g_k}$ (see Corollary 1). Therefore the variables $\underline{e}(t)$ and $\overline{e}(t)$ are bounded for the dwell-time $T_k \in [T_{\min}, T_{\max}]$. We continue assuming the boundedness of the estimates $\bar{x}(t)$ and $\underline{x}(t)$, which follows boundedness of x claimed in Assumption 1. From assumptions 2.ii and 2.iii we conclude that $\underline{e}(t) \geq 0$ and $\overline{e}(t) \geq 0$ ($\underline{g_1}, \overline{g_1}, \underline{g_2}, \overline{g_2}$ have the same property and $\underline{e}(0) \geq 0$ and $\overline{e}(0) \geq 0$ by conditions, then the result follows combining the theories presented in subsections 1.4 and 1.5). That implies the required order relation $\underline{x}(t) \leq x(t) \leq \bar{x}(t)$ is satisfied for all $t \in \mathbb{R}_+$. □

The imposed requirement, that the matrices $A - LC$ and $G - MC$ are Metzler and nonnegative respectively, is rather restrictive. In order to relax assumptions 2.ii and 2.iii, let us suggest the following.

Assumption 4. *There exist a Metzler matrix R, a matrix $T \in \mathbb{R}_+^{n\times n}$ and a matrix $P \in S_{\succ 0}^n$ such that the LMI*

$$T^{\mathrm{T}} e^{R^{\mathrm{T}}\theta} P e^{R\theta} T - P \prec 0 \tag{2.7}$$

is satisfied for all $\theta \in [T_{\min}, T_{\max}]$.

There exist a matrix $L \in \mathbb{R}^{n\times p}$ and a matrix $M \in \mathbb{R}^{n\times p}$ such that $\lambda(A - LC) = \lambda(R)$, $\lambda(G - MC) = \lambda(T)$, the pairs $(A - LC, e_1)$, (R, e_2), $(G - MC, e_3)$, (T, e_4) are observable for some $e_j \in \mathbb{R}^{1\times n}$ with $j = \overline{1, 4}$.

When Assumption 4 holds, the quadratic form $V(x) = x^{\mathrm{T}} P x$ is a Lyapunov function for linear discrete-time system $z_{i+1} = e^{R\theta} T z_i$ for all $\theta \in [T_{\min}, T_{\max}]$ and $i \in \mathbb{Z}_+$ by Theorem 1. In addition, comparing with assumptions 2.ii and 2.iii, in Assumption 4 it is proposed that the matrices $A - LC$ and $G - MC$ are similar to given Metzler and nonnegative matrices R and T respectively [40], with differing similarity transformation matrices $S_1 \in \mathbb{R}^{n\times n}$ and $S_2 \in \mathbb{R}^{n\times n}$ (*i.e.* $S_1^{-1}(A - LC)S_1 = R$ and $S_2^{-1}(G - MC)S_2 = T$). The key idea of the following design of an interval observer is how to combine these different transformations of coordinate S_1 and S_2 (denote $S = (S_1^{-1} S_2)^{-1}$), without introducing an auxiliary restriction.

Theorem 3. *Let assumptions 1, 3 and 4 be satisfied. Then for all* $t \in \mathbb{R}_+$ *the estimates* $\underline{x}(t)$ *and* $\bar{x}(t)$ *are bounded and*

$$\underline{x}(t) \leq x(t) \leq \bar{x}(t)$$

provided that $\underline{x}(0) \leq x(0) \leq \bar{x}(0)$, *where for all* $i \in \mathbb{Z}_+$*:*

$$\begin{aligned}
\underline{x}(t) &= S_1^+ \underline{z_1}(t) - S_1^- \overline{z_1}(t), \\
\bar{x}(t) &= S_1^+ \overline{z_1}(t) - S_1^- \underline{z_1}(t), \\
\dot{\underline{z_1}}(t) &= R\underline{z_1}(t) + F_1 y(t) - \overline{F_1} V + (S_1^{-1})^+ \underline{b}(t) \\
&\quad -(S_1^{-1})^- \overline{b}(t)\ \forall t \in [t_i, t_{i+1}), \\
\underline{z_2}(t_{i+1}^-) &= S^+ \underline{z_1}(t_{i+1}^-) - S^- \overline{z_1}(t_{i+1}^-), \\
\underline{z_2}(t_{i+1}) &= T\underline{z_2}(t_{i+1}^-) + F_2 y(t_{i+1}) - \overline{F_2} V \\
&\quad +(S_2^{-1})^+ \underline{d}(t_{i+1}) - (S_2^{-1})^- \overline{d}(t_{i+1}), \\
\underline{z_1}(t_{i+1}) &= (S^{-1})^+ \underline{z_2}(t_{i+1}) - (S^{-1})^+ \overline{z_2}(t_{i+1}), \\
\dot{\overline{z_1}}(t) &= R\overline{z_1}(t) + F_1 y(t) + \overline{F_1} V + (S_1^{-1})^+ \overline{b}(t) \\
&\quad -(S_1^{-1})^- \underline{b}(t)\ \forall t \in [t_i, t_{i+1}), \\
\overline{z_2}(t_{i+1}^-) &= S^+ \overline{z_1}(t_{i+1}^-) - S^- \underline{z_1}(t_{i+1}^-), \\
\overline{z_2}(t_{i+1}) &= T\overline{z_2}(t_{i+1}^-) + F_2 y(t_{i+1}) + \overline{F_2} V \\
&\quad +(S_2^{-1})^+ \overline{d}(t_{i+1}) - (S_2^{-1})^- \underline{d}(t_{i+1}), \\
\overline{z_1}(t_{i+1}) &= (S^{-1})^+ \overline{z_2}(t_{i+1}) - (S^{-1})^+ \underline{z_2}(t_{i+1}), \\
\underline{z_1}(0) &= (S_1^{-1})^+ \underline{x}(0) - (S_1^{-1})^- \overline{x}(0), \\
\overline{z_1}(0) &= (S_1^{-1})^+ \overline{x}(0) - (S_1^{-1})^- \underline{x}(0), \\
\underline{z_2}(0) &= (S_2^{-1})^+ \underline{x}(0) - (S_2^{-1})^- \overline{x}(0), \\
\overline{z_1}(0) &= (S_2^{-1})^+ \overline{x}(0) - (S_2^{-1})^- \underline{x}(0),
\end{aligned} \tag{2.8}$$

where $F_1 = S_1^{-1}L$, $\overline{F_1} = |F_1|E_{p\times 1}$, $F_2 = S_2^{-1}M$ *and* $\overline{F_2} = |F_2|E_{p\times 1}$.

Proof. Consider the system (2.1) in the new coordinates $z_1 = S_1^{-1}x$,

$z_2 = S_2^{-1}x$, $z_1 = S^{-1}z_2$:

$$\begin{aligned}
\dot{z}_1(t) &= Rz_1(t) + F_1[y(t) - v(t)] \\
&\quad + S_1^{-1}b(t)\ \forall t \in [t_i, t_{i+1}), \\
z_2(t_{i+1}) &= Tz_2(t_{i+1}^-) + F_2[y(t_{i+1}) - v(t_{i+1})] \\
&\quad + S_2^{-1}d(t_{i+1}), \\
y(t) &= CS_1z_1(t) + v(t)\ \forall t \in [t_i, t_{i+1}), \\
y(t_{i+1}) &= CS_2z_2(t_{i+1}) + v(t_{i+1}), \\
z_2(t_{i+1}) &= (S^+ - S^-)z_1(t_{i+1}).
\end{aligned}$$

The dynamics of the errors $\underline{e_1}(t) = z_1(t) - \underline{z_1}(t)$, $\overline{e_1}(t) = \overline{z_1}(t) - z_1(t)$, $\underline{e_2}(t) = z_2(t) - \underline{z_2}(t)$, $\overline{e_2}(t) = \overline{z_2}(t) - z_2(t)$ obey the equations for all $i \in \mathbb{Z}_+$:

$$\begin{aligned}
\dot{\underline{e_1}}(t) &= R\underline{e_1}(t) + \underline{g_1}(t)\ \forall t \in [t_i, t_{i+1}), \\
\underline{e_2}(t_{i+1}^-) &= S^+\underline{e_1}(t_{i+1}^-) + S^-\overline{e_1}(t_{i+1}^-), \\
\underline{e_2}(t_{i+1}) &= T\underline{e_2}(t_{i+1}^-) + \underline{g_2}(t_{i+1}), \\
\underline{e_1}(t_{i+1}) &= (S^{-1})^+\underline{e_2}(t_{i+1}) + (S^{-1})^-\overline{e_2}(t_{i+1}), \\
\dot{\overline{e_1}}(t) &= R\overline{e_1}(t) + \overline{g_1}(t)\ \forall t \in [t_i, t_{i+1}), \\
\overline{e_2}(t_{i+1}^-) &= S^+\overline{e_1}(t_{i+1}^-) + S^-\underline{e_1}(t_{i+1}^-), \\
\overline{e_2}(t_{i+1}) &= T\overline{e_2}(t_{i+1}^-) + \overline{g_2}(t_{i+1}), \\
\overline{e_1}(t_{i+1}) &= (S^{-1})^+\overline{e_2}(t_{i+1}) + (S^{-1})^-\underline{e_2}(t_{i+1}),
\end{aligned} \tag{2.9}$$

where

$$\begin{aligned}
\underline{g_1}(t) &= [\overline{F_1}V - F_1v(t)] + [(S_1^{-1})b(t) \\
&\quad - (S_1^{-1})^+\underline{b}(t) + (S_1^{-1})^-\overline{b}(t)], \\
\underline{g_2}(t_{i+1}) &= [\overline{F_2}V - F_2v(t_{i+1})] + [(S_2^{-1})d(t_{i+1}) \\
&\quad - (S_2^{-1})^+\underline{d}(t_{i+1}) + (S_2^{-1})^-\overline{d}(t_{i+1})], \\
\overline{g_1}(t) &= [\overline{F_1}V + F_1v(t)] + [(S_1^{-1})^+\overline{b}(t) \\
&\quad - (S_1^{-1})^-\underline{b}(t) - (S_1^{-1})b(t)], \\
\overline{g_2}(t_{i+1}) &= [\overline{F_2}V + F_2v(t_{i+1})] + [(S_2^{-1})^+\overline{d}(t_{i+1}) \\
&\quad - (S_2^{-1})^-\underline{d}(t_{i+1}) - (S_2^{-1})d(t_{i+1})].
\end{aligned}$$

According to Assumption 3 we have $\underline{g_1}, \overline{g_1}, \underline{g_2}, \overline{g_2} \in \mathcal{L}_\infty$, $\underline{g_1}(t) \geq 0$, $\overline{g_1}(t) \geq 0$ $\forall t \in [t_i, t_{i+1})$ and $\underline{g_2}(t_{i+1}) \geq 0$, $\overline{g_2}(t_{i+1}) \geq 0$ $\forall i \geq 1$. The matrix R is Metzler, the matrix T is nonnegative and these two matrices verify the LMI (2.7) when Assumption 4 is satisfied. Therefore, the system (2.9) with ranged dwell-time $T_i \in [T_{\min}, T_{\max}]$ is asymptotically stable for $\underline{g_k} = \overline{g_k} = 0$, $k = 1, 2$ and it has bounded state variables for bounded $\underline{g_k}, \overline{g_k}$ (see Corollary 1), then the variables $\underline{e_1}(t)$, $\overline{e_1}(t)$, $\underline{e_2}(t)$ and $\overline{e_2}(t)$ are bounded. Next, from Assumption 1 ($z(t)$ and $x(t)$ are bounded), we obtain boundedness of the estimates $\overline{z_1}(t)$, $\underline{z_1}(t)$, $\overline{z_2}(t)$, $\underline{z_2}(t)$ and, hence, boundedness of $\bar{x}(t)$, $\underline{x}(t)$. From the structure of the interval observer (2.8) and Assumption 4, since the matrix R is Metzler and the matrix T is nonnegative, we conclude that $\underline{e_1}(t) \geq 0$, $\overline{e_1}(t) \geq 0$, $\underline{e_2}(t) \geq 0$ and $\overline{e_2}(t) \geq 0$ ($\underline{g_1}, \overline{g_1}, \underline{g_2}, \overline{g_2}$ have the same property, $\underline{e_1}(0) \geq 0$, $\overline{e_1}(0) \geq 0$, $\underline{e_2}(0) \geq 0$ and $\overline{e_2}(0) \geq 0$ by construction, and the result follows combining the theories presented in subsections 1.4 and 1.5). Thus, from the definitions of errors we conclude that for all $i \in \mathbb{Z}_+$:

$$\underline{z_1}(t) \leq z_1(t) \leq \overline{z_1}(t) \; \forall t \in [t_i, t_{i+1}),$$
$$\underline{z_2}(t_{i+1}) \leq z_2(t_{i+1}) \leq \overline{z_2}(t_{i+1}) \; \forall i \geq 1,$$

which imply the relations of Theorem 3. □

There is another possibility for an interval observer construction avoiding the restrictions of Assumption 2, but with more conservative stability conditions. To this end, consider the following assumption.

Assumption 5. *There exist a matrix $L \in \mathbb{R}^{n\times p}$, a matrix $M \in \mathbb{R}^{n\times p}$ and a matrix $P \in S^n_{\succ 0}$ such that the LMI*

$$J^{\mathrm{T}} e^{U^{\mathrm{T}}\theta} P e^{U\theta} J - P \prec 0 \tag{2.10}$$

is satisfied for all $\theta \in [T_{\min}, T_{\max}]$ and $U = \begin{bmatrix} D_0 & D_1 \\ D_1 & D_0 \end{bmatrix}$, $J = \begin{bmatrix} (G-MC)_p & (G-MC)_n \\ (G-MC)_p & (G-MC)_n \end{bmatrix}$ for $A - LC = D_0 - D_1$ where D_0 is Metzler and $D_1, (G-MC)_p, (G-MC)_n \in \mathbb{R}^{n\times n}_+$.

Comparing with Assumption 4, here by construction the matrices

U and J are Metzler and nonnegative respectively, *i.e.* these matrices can always be constructed satisfying these properties for any $A-LC$ and $G-MC$ (a possible but not unique choice is $(G-MC)_p = (G-MC)^+$ and $(G-MC)_n = (G-MC)^-$, for example), then there is no need in transformations of coordinates S_1 and S_2. However, the main restriction is on the stability of such U and J, and the conditions of stability are formulated by LMI (2.10) following Theorem 1. The following result can be proven.

Theorem 4. *Let assumptions 1, 3 and 5 be satisfied. Then for all* $t \in \mathbb{R}_+$ *the estimates* $\underline{x}(t)$ *and* $\bar{x}(t)$ *are bounded and*

$$\underline{x}(t) \leq x(t) \leq \bar{x}(t)$$

provided that $\underline{x}(0) \leq x(0) \leq \bar{x}(0)$*, where for all* $i \in \mathbb{Z}_+$*:*

$$\begin{aligned}
\dot{\underline{x}}(t) &= D_0\underline{x}(t) - D_1\overline{x}(t) + Ly(t) + \underline{b}(t) \\
&\quad -\overline{L}V \ \forall t \in [t_i, t_{i+1}), \\
\underline{x}(t_{i+1}) &= (G-MC)_p\underline{x}(t_{i+1}^-) - (G-MC)_n\overline{x}(t_{i+1}^-) \\
&\quad +My(t_{i+1}) + \underline{d}(t_{i+1}) - \overline{M}V, \\
\dot{\overline{x}}(t) &= D_0\overline{x}(t) - D_1\underline{x}(t) + Ly(t) + \overline{b}(t) \\
&\quad +\overline{L}V \ \forall t \in [t_i, t_{i+1}), \\
\overline{x}(t_{i+1}) &= (G-MC)_p\overline{x}(t_{i+1}^-) - (G-MC)_n\underline{x}(t_{i+1}^-) \\
&\quad +My(t_{i+1}) + \overline{d}(t_{i+1}) + \overline{M}V,
\end{aligned} \tag{2.11}$$

where $\overline{L} = |L|E_{p\times 1}$ *and* $\overline{M} = |M|E_{p\times 1}$*.*

Proof. The equation (2.1) can be rewritten as follows for all $i \in \mathbb{Z}_+$:

$$\begin{aligned}
\dot{x}(t) &= (A-LC)x(t) + L[y(t) - v(t)] \\
&\quad +b(t) \ \forall t \in [t_i, t_{i+1}), \\
x(t_{i+1}) &= (G-MC)x(t_{i+1}^-) \\
&\quad +M[y(t_{i+1}) - v(t_{i+1})] + d(t_{i+1}).
\end{aligned}$$

Then the dynamics of the errors $\underline{e}(t) = x(t) - \underline{x}(t)$, $\overline{e}(t) = \overline{x}(t) - x(t)$ obey the equations:

$$
\begin{aligned}
\dot{\underline{e}}(t) &= D_0\underline{e}(t) + D_1\overline{e}(t) + \underline{g_1}(t)\ \forall t \in [t_i, t_{i+1}), \\
\underline{e}(t_{i+1}) &= (G - MC)_p\underline{e}(t_{i+1}^-) \\
&\quad +(G - MC)_n\overline{e}(t_{i+1}^-) + \underline{g_2}(t_{i+1}), \\
\dot{\overline{e}}(t) &= D_0\overline{e}(t) + D_1\underline{e}(t) + \overline{g_1}(t)\ \forall t \in [t_i, t_{i+1}), \\
\overline{e}(t_{i+1}) &= (G - MC)_p\overline{e}(t_{i+1}^-) \\
&\quad +(G - MC)_n\underline{e}(t_{i+1}^-) + \overline{g_2}(t_{i+1}),
\end{aligned}
\tag{2.12}
$$

where

$$
\begin{aligned}
\underline{g_1}(t) &= [\overline{L}V - Lv(t)] + [b(t) - \underline{b}(t)], \\
\underline{g_2}(t_{i+1}) &= [\overline{M}V - Mv(t_{i+1})] + [d(t_{i+1}) - \underline{d}(t_{i+1})], \\
\overline{g_1}(t) &= [\overline{L}V + Lv(t)] + [\overline{b}(t) - b(t)], \\
\overline{g_2}(t_{i+1}) &= [\overline{M}V + Mv(t_{i+1})] + [\overline{d}(t_{i+1}) - d(t_{i+1})].
\end{aligned}
$$

According to Assumption 3 we have $\underline{g_1}, \overline{g_1}, \underline{g_2}, \overline{g_2} \in \mathcal{L}_\infty$, $\underline{g_1}(t) \geq 0$, $\overline{g_1}(t) \geq 0$ $\forall t \in [t_i, t_{i+1})$ and $\underline{g_2}(t_{i+1}) \geq 0$, $\overline{g_2}(t_{i+1}) \geq 0$ $\forall i \geq 1$. If Assumption 5 is satisfied, then system (2.12) with ranged dwell-time $T_i \in [T_{\min}, T_{\max}]$ is asymptotically stable for $\underline{g_k} = \overline{g_k} = 0$, $k = 1, 2$ and it has bounded state variables for bounded $\underline{g_k}, \overline{g_k}$ (from Corollary 1). Therefore the variables $\underline{e}(t)$ and $\overline{e}(t)$ are bounded, and the estimates $\bar{x}(t)$, $\underline{x}(t)$ inherit the same property due to Assumption 1. From the interval observer (2.11) structure and Assumption 5, since the matrix U is Metzler and the matrix J is nonnegative (D_0 is Metzler and $D_1, (G - MC)_p, (G - MC)_n \in \mathbb{R}_+^{n\times n}$), we obtain that $\underline{e}(t) \geq 0$ and $\overline{e}(t) \geq 0$ ($\underline{g_1}, \overline{g_1}, \underline{g_2}, \overline{g_2}$ have the same property, $\underline{e}(0) \geq 0$ and $\overline{e}(0) \geq 0$ by construction, and the result follows combining the theories presented in subsections 1.4 and 1.5). Consequently, the required order relation $\underline{x}(t) \leq x(t) \leq \bar{x}(t)$ is satisfied for all $t \in \mathbb{R}_+$. □

The results of theorems 3 and 4 can be combined, *i.e.* only one transformation S_1 or S_2 can be used together with the decomposition from Assumption 5.

2.4 Examples

In this section, we present three examples. The first and the third examples are academic hybrid linear systems and the second one is a bouncing ball.

2.4.1 Academic hybrid linear system

Consider the following system:

$$\begin{aligned}
\dot{x}(t) &= Ax(t) + b(t) \;\forall t \in [0,\, 5) \cup (5,\, 10) \cup (10, +\infty), \\
x(t) &= Gx(t^-) + d(t) \;\forall t \in \{5,\, 10\}, \\
y(t) &= Cx(t) + v(t),
\end{aligned}$$

where the matrices A, C and G are defined as follows [4]:

$$A = \begin{bmatrix} -1 & 0 \\ 1 & -2 \end{bmatrix},\; C = \begin{bmatrix} 0 & 1 \end{bmatrix},\; G = \begin{bmatrix} 2 & 1 \\ 1 & 3 \end{bmatrix},$$

and $x(t) \in \mathbb{R}^2$, $y(t) \in \mathbb{R}$ are the state and the output respectively. The signals $b(t)$, $d(t)$ and $v(t)$ are:

$$b(t) = \begin{bmatrix} \beta \sin(t) \\ \beta \sin(t) \end{bmatrix},\; d(t) = \begin{bmatrix} \delta \sin(t) \\ \delta \sin(t) \end{bmatrix},\; v(t) = V \sin(t),$$

where $\beta = 0.1$, $\delta = 0.3$ and $V = 0.03$ are known parameters. Thus,

$$\begin{aligned}
\underline{b}(t) &= \begin{bmatrix} -\beta \\ -\beta \end{bmatrix},\; \overline{b}(t) = \begin{bmatrix} \beta \\ \beta \end{bmatrix}, \\
\underline{d}(t) &= \begin{bmatrix} -\delta \\ -\delta \end{bmatrix},\; \overline{d}(t) = \begin{bmatrix} \delta \\ \delta \end{bmatrix}.
\end{aligned}$$

Assumption 3 is then satisfied. Assume that $||x|| < +\infty$ and Assumption 1 is valid. Assumption 2.ii is verified for $L = \begin{bmatrix} 0 & 1 \end{bmatrix}^{\mathrm{T}}$: the matrix $A - LC = \begin{bmatrix} -1 & 0 \\ 1 & -3 \end{bmatrix}$ is Metzler. Assumption 2.iii is verified for

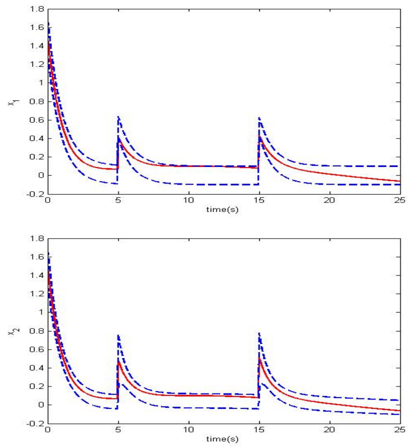

Figure 2.1: Results of the simulation for the academic linear impulsive system

$M = \begin{bmatrix} 1 & 2.8 \end{bmatrix}^{\mathrm{T}}$: the matrix $G - MC = \begin{bmatrix} 2 & 0 \\ 1 & 0.2 \end{bmatrix}$ is nonnegative but not Schur stable. By applying Matlab YALMIP toolbox [28] to solve the LMI (2.3), we found that Assumption 2.i holds for all $\theta \in [0.6580, +\infty)$. Then the dynamics of the errors $\underline{e}(t) = x(t) - \underline{x}(t)$, $\overline{e}(t) = \overline{x}(t) - x(t)$ with ranged dwell-time $\theta \in [0.6580, +\infty)$ are ISS. Therefore all conditions of Theorem 2 are satisfied and the interval observer (2.4) solves the problem of interval state estimation. The results of simulation are shown in Fig 2.1, where the solid lines represent the states x_k, $k = 1, 2$ and the dash lines are used for the interval estimates $\underline{x_k}$ and $\overline{x_k}$.

2.4.2 Bouncing ball

Consider the case of vertical motion of a ball under gravity with a constant acceleration g. The dynamics are given by

$$\dot{p}(t) = v(t); \ \dot{v}(t) = -g,$$

where $p(t) \in \mathbb{R}_+$ is the position of the ball and $v(t) \in \mathbb{R}$ is its velocity, which is assumed to be downward. Upon hitting the ground at instant of time $t' \geq 0$ with $p(t') = 0$, we instantly set $v(t')$ to -$\rho v(t'^-)$, where $\rho \in [0, 1]$ is the coefficient of restitution. In general, this model can be presented in the form of system (2.1):

$$
\begin{aligned}
x(t) &= [p(t)\ v(t)]^{\mathrm{T}}, \\
\dot{x}(t) &= Ax(t) + b(t) \text{ when } x_1(t) \neq 0, \\
x(t) &= Gx(t^-) + d(t) \text{ when } x_1(t) = 0, \\
y(t) &= Cx(t),
\end{aligned}
$$

where $A = \begin{bmatrix} 0 & 1 \\ 0 & 0 \end{bmatrix}$, $C = \begin{bmatrix} 1 & 0 \end{bmatrix}$, $G = \begin{bmatrix} 1 & 0 \\ 0 & -\rho \end{bmatrix}$; $x(t) \in \mathbb{R}^2$, $y(t) \in \mathbb{R}$ are respectively the state and the output; the signals $b(t)$ and $d(t)$ model some additional perturbing forces applied to the ball:

$$
b(t) = \begin{bmatrix} \beta \sin(t) \\ -g + \beta \sin(t) \end{bmatrix}, \ d(t) = \begin{bmatrix} \delta \sin(t) \\ \delta \sin(t) \end{bmatrix},
$$

where $\beta = 0.5$ and $\delta = 0.5$ are known parameters. Thus,

$$
\underline{b}(t) = \begin{bmatrix} -\beta \\ -g - \beta \end{bmatrix}, \ \overline{b}(t) = \begin{bmatrix} \beta \\ -g + \beta \end{bmatrix},
$$
$$
\underline{d}(t) = \begin{bmatrix} -\delta \\ -\delta \end{bmatrix}, \ \overline{d}(t) = \begin{bmatrix} \delta \\ \delta \end{bmatrix}
$$

and Assumption 3 is then satisfied. Assume that $||x|| < +\infty$ (Assumption 1 is valid). Verifying the LMI (2.7) with Matlab YALMIP toolbox [28], we found that Assumption 4 holds for all ranged dwell-time $T_k > 0$. Therefore, all conditions of Theorem 3 are satisfied. Finally, the matrices

$$
R = \begin{bmatrix} -2 & 0 \\ 0 & -1 \end{bmatrix}, \ S_1 = \begin{bmatrix} -0.7071 & -0.4472 \\ -0.7071 & -0.8944 \end{bmatrix},
$$
$$
T = \begin{bmatrix} -0.8 & 0 \\ 0 & 0.9 \end{bmatrix}, \ S_2 = \begin{bmatrix} 0 & 0.9594 \\ 1 & 0.2822 \end{bmatrix}
$$

satisfy all conditions of Theorem 3 and the interval observer (2.8) solves the problem of interval state estimation for bouncing ball. The results of simulation are shown in Fig 2.2, where the solid lines

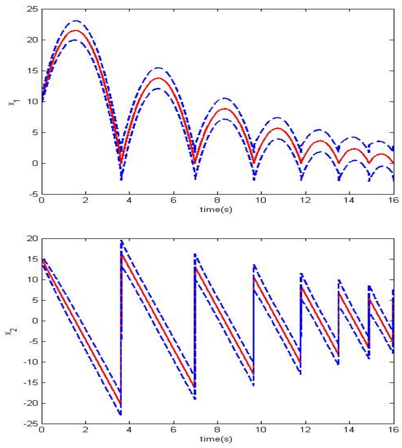

Figure 2.2: Results of the simulation for the bouncing ball model

represent the states x_k, $k = 1, 2$ and the dash lines are used for the interval estimates $\underline{x_k}$ and $\overline{x_k}$.

Remark 1. In the example of the bouncing ball considered in this work, the measurement noise is equal to zero. This means the times of the jumps in the state are well estimated as the output signal is supposed to be perfect (without noise). In the real case, there is always a measurement noise in the output signal: the jumps times in the state are not known and need to be estimated. It introduces a time-delay in the estimated jumping time and causes some additional error in the state estimation.

2.4.3 Academic linear impulsive system

Consider the following system:

$$
\begin{aligned}
\dot{x}(t) &= Ax(t) + b(t) \ \forall t \in [0,\ 5) \cup (5,\ 10) \cup (10, +\infty), \\
x(t) &= Gx(t^-) + d(t) \ \forall t \in \{5,\ 10\}, \\
y(t) &= Cx(t),
\end{aligned}
$$

where the matrices A, C and G are defined as follows:

$$
A = \begin{bmatrix} -2 & 0 \\ -4 & -3 \end{bmatrix}, \ C = \begin{bmatrix} 0 & 1 \end{bmatrix}, \ G = \begin{bmatrix} 2 & 0 \\ 1 & -0.2 \end{bmatrix}
$$

and $x(t) \in \mathbb{R}^2$, $y(t) \in \mathbb{R}$ are respectively the state and the output. The signals $b(t)$ and $d(t)$ are:

$$b(t) = \begin{bmatrix} \beta\sin(2t)\cos(t) \\ \beta\sin(2t)\cos(t) \end{bmatrix}, \; d(t) = \begin{bmatrix} 0.2 + \delta\sin(t) \\ 0.2 + \delta\sin(t) \end{bmatrix}$$

with known $\beta = 0.1$ and $\delta = 0.1$. Thus,

$$\underline{b}(t) = \begin{bmatrix} -\beta \\ -\beta \end{bmatrix}, \; \overline{b}(t) = \begin{bmatrix} \beta \\ \beta \end{bmatrix},$$
$$\underline{d}(t) = \begin{bmatrix} -\delta + 0.2 \\ -\delta + 0.2 \end{bmatrix}, \; \overline{d}(t) = \begin{bmatrix} \delta + 0.2 \\ \delta + 0.2 \end{bmatrix}.$$

Assumption 3 is then satisfied. Assume that $||x|| < +\infty$ and Assumption 1 is valid. There is no observer gain L such that the matrix $A - LC$ is Metzler. For $L = \begin{bmatrix} 0 & -2 \end{bmatrix}^{\mathrm{T}}$ and $A - LC = \begin{bmatrix} -2 & 0 \\ -4 & -1 \end{bmatrix}$, we choose

$$D_0 = \begin{bmatrix} -1.5 & 0 \\ 0 & -1 \end{bmatrix}, \; D_1 = \begin{bmatrix} 0.5 & 0 \\ 4 & 0 \end{bmatrix},$$

then D_0 is Metzler and $D_1 \in \mathbb{R}_+^{n\times n}$. For $M = \begin{bmatrix} -1 & 2.8 \end{bmatrix}^{\mathrm{T}}$ and $G - MC = \begin{bmatrix} 2 & 1 \\ 1 & -3 \end{bmatrix}$, we choose:

$$(G - MC)_p = \begin{bmatrix} 2.5 & 1 \\ 1 & 0 \end{bmatrix}, \; (G - MC)_n = \begin{bmatrix} 0.5 & 0 \\ 0 & 3 \end{bmatrix}.$$

$(G - MC)_p \in \mathbb{R}_+^{n\times n}$ and $(G - MC)_n \in \mathbb{R}_+^{n\times n}$. Note that the matrix $G - MC$ is negative and is not Schur stable . By applying Matlab YALMIP toolbox [28] to solve the LMI (2.10), we found that Assumption 5 holds for all $T_k \in (2.7579, +\infty)$. Therefore, all conditions of Theorem 4 are satisfied and the interval observer (2.11) solves the problem of interval state estimation. The results of simulation are shown in Fig 2.3, where the solid lines represent the states x_k, $k = 1, 2$ and the dash lines are used for the interval estimates $\underline{x_k}$ and $\overline{x_k}$.

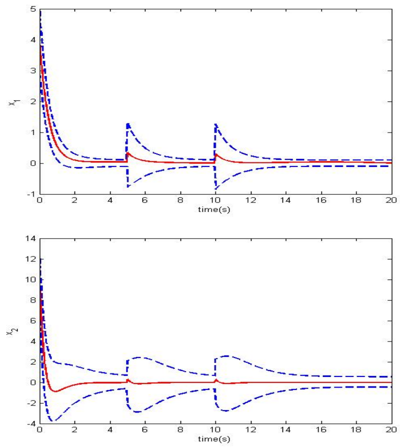

Figure 2.3: Results of the simulation for the academic linear impulsive system

2.5 Conclusion

A long this chapter, interval observers are proposed for different kinds of hybrid linear systems. The efficiency of these techniques is shown on examples of computer simulation for two academic systems and a bouncing ball. The problem of interval estimation of sequestred infected erythrocytes in plasmodium falciparum malaria patients will be discussed in the next chapter.

Chapter 3

Interval estimation of sequestred infected erythrocytes in plasmodium falciparum malaria patients

3.1 Introduction

Malaria is a disease that causes at least one million deaths around the world each year, with ninety percents among African children, and it is spreed by the *Plasmodium* parasite. The most dangerous type of malaria is summoned by the most virulent species called *Plasmodium falciparum*. Sequestration is one of the characteristics of *Plasmodium falciparum*, which is related with the *Plasmodium* life cycle. The cycle begins when a parasite enters the human body through the bite of an infected mosquito, after which it migrates to the liver and starts to multiply within. The free forms resulting from this multiplication (called merozoites) are able to invade the red blood cells (erythrocytes). The infected erythrocytes are matured during the erythrocytic cycle. At roughly the middle stage of trophozoite development (in 24 hours), molecules on the surface of infected erythrocytes can link to receptors of endothelial cells. This bind has the effect of holding infected erythrocytes within vessels of organs (such as the brain), where they remain until the rupture of the erythrocyte and the release of merozoites. This period of attachment is called sequestration and during it, the infected erythrocytes are not detectable in the blood flow, they are "sequestered". Also it is widely accepted that antimalarial drugs act preferentially on different stages of parasite development [21, 20].

In practice, to know the stage of infection for a patient, the total parasite concentration $\sum_{i=1}^{n} y_i$ in the bloodstream is needed, where y_i represent population of parasites of certain age, from the youngest y_1 till the oldest y_n, $n < 1$ determines the grid of age differentiation. However, only the peripheral infected erythrocytes, *i.e.* the young parasites $y_1 + y_2 + ...y_k$ for some $k < n$, also called circulating, can be observed (seen on peripheral blood smears) and the other ones (sequestered $y_{k+1}, ...y_n$) are hidden in some organs like brain and heart, and cannot be observed. There is no clinical method of measuring the sequestered infected cells directly.

That is why the estimation of sequestered parasite population has been a challenge for the biologist and modeler, with many authors having studied this problem [21, 20, 37, 2]. In this work an interval observer is designed in order to estimate the admissible interval for sequestered parasite population. In the presence of uncertainty, which has an important impact in this application, design of a conventional estimator, converging to the ideal value of the state, cannot be realized. In this case an interval estimation becomes more feasible: an observer can be constructed that, using input-output information, evaluates the set of admissible values (interval) for the state at each instant of time. The interval length is proportional to the size of the model uncertainty (it has to be minimized by tuning the observer parameters). There are several approaches to design interval/set-membership estimators [24, 25, 38]. This section is devoted to interval observers, which form a subclass of set-membership estimators and whose design is based on the monotone systems theory [38, 36, 41, 40, 7].

3.2 Estimation of the hidden parasitized erythrocytes

The exact number of stages of parasitized erythrocytes is generally unknown but one can distinguish five main stages by simple morphology: young ring, old ring, trophozoite, early schizont and nally late schizont [2]. Thus one can assume that the parasitized erythrocytes population within the host is divided in 5 different stages: $y_1; y_2; y_3; y_4; y_5$. The two first stages correspond to the concentration of free circulating parasitized erythrocytes and the three last stages stand for the sequestered ones. The healthy cells x are produced by a constant recruitment Λ from the thymus and they become infected by an effective contact with a merozoite m. At the late stage of infected cells, the erythrocyte ruptures and releases r merozoites.

It is assumed that the circulating parasitaemia, i.e: $y_1 + y_2$ can be measured and the aim of this work is to find an estimate of the sequestered parasitaemia, $y_3 + y_4 + y_5$. To describe the dynamics of the parasitized erythrocytes, we use the following system [2]:

$$\begin{aligned} \dot{z}(t) &= A(t)z(t) + E\beta(t)x(t)m(t) + e_1\Lambda(t) \ \forall t \geq 0, \\ Y(t) &= Cz(t) + v(t), \end{aligned} \tag{3.1}$$

where $z = (x, y_1, \dots, y_5, m)^{\mathrm{T}} \in \mathbb{R}^7_+$ is the state vector and $Y \in \mathbb{R}_+$ is the measured output, $v \in \mathcal{L}_\infty$ is the measurement noise, $||v||_\infty \leq V$ for some known $V > 0$; y_1 and y_2 correspond to the concentrations of free circulating parasitized erythrocytes and y_3, y_4, y_5 correspond to the sequestered ones; x is the concentration of healthy cells, and m is the concentration of merozoites; $\Lambda(t) \in \mathbb{R}_+$, $\Lambda \in \mathcal{L}_\infty$ represents recruitment of the healthy red blood cells (RBC) and $\beta(t) \in \mathbb{R}_+$, $\beta \in \mathcal{L}_\infty$ is the rate of infection of RBC by merozoites. The variables $\beta(t)$ and $\Lambda(t)$ serve as exogenous uncertain inputs in (3.1). The time-varying matrix A and constant matrices C, E, e_1 are defined as follows:

$$C = [\ 0 \quad 1 \quad 1 \quad 0 \quad 0 \quad 0 \quad 0\ ],$$
$$E = [\ -1 \quad 1 \quad 0 \quad 0 \quad 0 \quad 0 \quad -1\ ]^{\mathrm{T}},$$
$$e_1 = [\ 1 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0\ ]^{\mathrm{T}},$$

$$A = \begin{bmatrix} -\mu_x & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu_1 - \gamma_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma_1 & -\mu_2 - \gamma_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_2 & -\mu_3 - \gamma_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & \gamma_3 & -\mu_4 - \gamma_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma_4 & -\mu_5 - \gamma_5 & 0 \\ 0 & 0 & 0 & 0 & 0 & r\gamma_5 & -\mu_m \end{bmatrix},$$

where $\mu_x > 0$ is the natural death rate of healthy cells; $\mu_i > 0$ is the natural death rate of i^{th} stage of infected cells, $\gamma_i > 0$ is the transition rate from i^{th} stage to $(i+1)^{\text{th}}$ stage of infected cells, $i = 1, \ldots, 5$; $r > 0$ is the number of merozoites released by the late stage of infected cells, $\mu_m > 0$ is the natural death rate of merozoites.

For different patients the values of the parameters μ_x, μ_i, γ_i, r and μ_x are different and they are varying with time for a patient, that is why we assume that

$$\underline{A} \leq A(t) \leq \overline{A}$$

for some known $\underline{A}, \overline{A} \in \mathbb{R}^{7\times 7}$ and the instant value of $A(t)$ is unavailable. Similarly for the healthy RBC recruitment $\Lambda(t)$, the values $\underline{\Lambda}, \overline{\Lambda} \in \mathbb{R}_+$ are given such that

$$\underline{\Lambda} \leq \Lambda(t) \leq \overline{\Lambda}\ \forall t \geq 0.$$

It is assumed that for $\beta(t)$ there is no confidence interval.

We suppose that $Y = y_1 + y_2 + v(t)$, *i.e.* the circulating *Plasmodium* can be measured with a noise v, while it is required to estimate the sequestered one $Z = y_3 + y_4 + y_5$.

3.3 Interval observer design

We define $w(t) = \beta(t)x(t)m(t)$ as a new unmeasurable variable, which can be considered as a new uncertain input for (3.1). Following [2] and using the equation (3.1), we can find:

$$w = ((CE)^{\mathrm{T}}CE)^{-1}(CE)^{\mathrm{T}}(\dot{Y} - CAz - Ce_1\Lambda)$$

where $\dot{Y}$ is the derivative of the output. Using Lemma 3 and differentiator (1.3), an estimate $\hat{\dot{Y}}$ of $\dot{Y}$ can be calculated such that for all $t \geq 0$:

$$\dot{Y}(t) = \hat{\dot{Y}}(t) + v'(t),$$

where $||v'||_\infty < V'$ for some known $V' > 0$.

Note that $CE = 1$, let $0 \leq \underline{z}(t) \leq z(t) \leq \overline{z}(t)$ for all $t \geq 0$ and some $\underline{z}, \overline{z} \in \mathbb{R}^7$, then using Lemma 1 we obtain the following relations for all $t \geq 0$:

$$\underline{w}(t) \leq w(t) \leq \overline{w}(t),$$

where $\underline{w} = \hat{\dot{Y}} - V' - Ce_1\overline{\Lambda} - (C\overline{A})^+\overline{z} + (C\overline{A})^-\underline{z}$ and $\overline{w} = \hat{\dot{Y}} + V' - Ce_1\underline{\Lambda} - (C\underline{A})^+\underline{z} + (C\underline{A})^-\overline{z}$.

Following [5] equations of an interval observer for (3.1) take the form:

$$\begin{aligned}
\dot{\underline{\zeta}}(t) &= \underline{A}\underline{\zeta}(t) + e_1\underline{\Lambda} + E^+\underline{w}(t) \\
&\quad -E^-\overline{w}(t) + \underline{L}(Y(t) - C\underline{\zeta}(t)) - |\underline{L}|V, \\
\dot{\overline{\zeta}}(t) &= \overline{A\zeta}(t) + e_1\overline{\Lambda} + E^+\overline{w}(t) \\
&\quad -E^-\underline{w}(t) + \overline{L}(Y(t) - C\overline{\zeta}(t)) + |\underline{L}|V, \\
&\quad \underline{z}(t) = \max\{0, \underline{\zeta}(t)\}, \\
&\quad \overline{z}(t) = \max\{0, \overline{\zeta}(t)\},
\end{aligned} \tag{3.2}$$

where $\underline{z} \in \mathbb{R}^7$ and $\overline{z} \in \mathbb{R}^7$ are respectively the lower and the upper interval estimates for the state z; $\underline{\zeta}, \overline{\zeta} \in \mathbb{R}^7$ is the state of (3.2). The following restrictions are imposed on (3.2):

Assumption 6. *There exist matrices $\overline{L} \in \mathbb{R}^{7\times1}$, $\underline{L} \in \mathbb{R}^{7\times1}$ such that the* *matrices* $(\overline{A} - \overline{L}C)$ *and* $(\underline{A} - \underline{L}C)$ *are Metzler.*

Assumption 6 fixes the main conditions to satisfy for positivity of the error dynamics (due to the structure of A this condition is always satisfied for $\overline{L} = \underline{L} = 0$).

Theorem 5. *Let Assumption 6 be satisfied. Then for all* $t \in \mathbb{R}_+$ *the estimates* $\underline{z}(t)$ *and* $\overline{z}(t)$ *given by (3.2) yield the relations:*

$$0 \leq \underline{z}(t) \leq z(t) \leq \bar{z}(t) \quad \forall t \geq 0, \tag{3.3}$$

provided that $0 \leq \underline{z}(0) \leq z(0) \leq \bar{z}(0)$*. If in addition, there exists a diagonal matrix* $P \in \mathbb{R}^{14}$ *and* $\gamma > 0$ *such that*

$$\mathcal{A}^T P + P\mathcal{A} + P(\gamma^{-2} I_{14} + FF^T)P + 2I_{14} \preceq 0$$

for

$$\mathcal{A} = \begin{bmatrix} (\underline{A} - \underline{L}C) & 0 \\ 0 & (\overline{A} - \overline{L}C) \end{bmatrix},$$

$$F = \begin{bmatrix} E^+(C\overline{A})^- + E^-(C\underline{A})^+ & -E^+(C\overline{A})^+ - E^-(C\underline{A})^- \\ -E^+(C\underline{A})^+ - E^-(C\overline{A})^- & E^+(C\underline{A})^- + E^-(C\overline{A})^+ \end{bmatrix},$$

then $\underline{z}, \bar{z} \in \mathcal{L}_\infty^7$ *(*$\underline{\zeta}, \bar{\zeta} \in \mathcal{L}_\infty^7$ *and the transfer function* $\begin{bmatrix} e_1\underline{\Lambda} + \underline{L}Y(t) - |\underline{L}|V \\ e_1\overline{\Lambda} + \overline{L}Y(t) + |\overline{L}|V, \end{bmatrix} \to \begin{bmatrix} \underline{\zeta} \\ \bar{\zeta} \end{bmatrix}$ *has* L_∞ *gain less than* γ*).*

Proof. Note that $z(t) \geq 0$ for all $t \geq 0$ and $z(t)$ is also bounded [2]. The equation (3.1) can be rewritten as follows:

$$\dot{z} = (A' - LC)z + (A(t) - A')z + Ew + e_1\Lambda + LY - Lv$$

for some $A' \in \mathbb{R}^{7\times 7}$ ($\underline{A}$ or $\overline{A}$) and $L \in \mathbb{R}^{7\times 1}$ ($\underline{L}$ or $\overline{L}$), then the dynamics of the errors $\underline{e}(t) = z(t) - \underline{\zeta}(t)$, $\overline{e}(t) = \overline{\zeta}(t) - z(t)$ obey the equations:

$$\begin{aligned} \dot{\underline{e}}(t) &= (\underline{A} - \underline{L}C)\underline{e}(t) + \underline{g}(t), \\ \dot{\overline{e}}(t) &= (\overline{A} - \overline{L}C)\overline{e}(t) + \overline{g}(t), \end{aligned} \tag{3.4}$$

where

$$\begin{aligned}\underline{g} &= (A(t)-\underline{A})z + Ew - E^{+}\underline{w} + E^{-}\overline{w} + \underline{L}v + |\underline{L}|V,\\ \overline{g} &= (\overline{A}-A(t))z + E^{+}\overline{w} - E^{-}\underline{w} - Ew - \overline{L}v + |\underline{L}|V.\end{aligned}$$

Under the introduced conditions, it can be inferred from Lemma 1 that $\underline{g}(t) \geq 0$, $\overline{g}(t) \geq 0$ $\forall t \geq 0$. From Assumption 6, we conclude that $\underline{e}(t) \geq 0$ and $\overline{e}(t) \geq 0$ ($\underline{g}, \overline{g}$ have the same property and $\underline{e}(0) \geq 0$ and $\overline{e}(0) \geq 0$ by conditions). That implies that the order relation $\underline{\zeta}(t) \leq z(t) \leq \bar{\zeta}(t)$ is satisfied for all $t \geq 0$, then (3.3) is true by construction of $\underline{z}, \overline{z}$ and due to nonnegativity of z.

In order to prove boundedness, let us define:

$$\begin{aligned}\zeta &= [\underline{\zeta}^{\mathrm{T}}\ \overline{\zeta}^{\mathrm{T}}]^{\mathrm{T}},\ \epsilon = [\underline{\epsilon}^{\mathrm{T}}\ \overline{\epsilon}^{\mathrm{T}}]^{\mathrm{T}},\\ \underline{\epsilon} &= Ce_1(E^{-}\underline{\Lambda} - E^{+}\overline{\Lambda}) + e_1\underline{\Lambda} + E\dot{\hat{Y}} - |E|V'\\ &\quad +\underline{L}Y - |\underline{L}|V,\\ \overline{\epsilon} &= Ce_1(E^{-}\overline{\Lambda} - E^{+}\underline{\Lambda}) + e_1\overline{\Lambda} + E\dot{\hat{Y}} + |E|V'\\ &\quad +\overline{L}Y + |\underline{L}|V,\end{aligned}$$

then dynamics of interval observer takes the form:

$$\dot{\zeta} = \mathcal{A}\zeta + F\max\{0,\zeta\} + \epsilon,$$

where the matrices $\mathcal{A}$ and F are defined in the theorem formulation and $\epsilon \in \mathcal{L}_{\infty}^{14}$ by construction. Consider a Lyapunov function $V(\zeta) = \zeta^{\mathrm{T}}P\zeta$, then

$$\begin{aligned}\dot{V} &= \zeta^{\mathrm{T}}(\mathcal{A}^{\mathrm{T}}P + P\mathcal{A})\zeta + 2\zeta^{\mathrm{T}}P[F\max\{0,\zeta\} + \epsilon]\\ &\leq \zeta^{\mathrm{T}}[\mathcal{A}^{\mathrm{T}}P + P\mathcal{A} + P(\gamma^{-2}I_{14} + FF^{\mathrm{T}})P + I_{14}]\zeta\\ &\quad +\gamma^{2}\epsilon^{\mathrm{T}}\epsilon\\ &\leq -\zeta^{\mathrm{T}}\zeta + \gamma^{2}\epsilon^{\mathrm{T}}\epsilon\end{aligned}$$

and the needed stability conclusion follows. □

The obtained interval estimates $\underline{z}, \overline{z}$ are nonnegative as the state

z is. Note that the presented approach can be easily extended to higher/lower order models of parasitized erythrocytes (when age partition of erythrocytes has more/less than 5 levels as in (3.1)).

Remark 2. In order to solve the matrix inequality introduced in Theorem 5 the following series of LMIs with respect to P can be used (it is obtained by application of the Schur complement):

$$\gamma^{-2}I_{14} + FF^{\mathrm{T}} \succ 0,$$
$$\begin{bmatrix} \left(\gamma^{-2}I_{14} + FF^{\mathrm{T}}\right)^{-1} & P \\ P & -\mathcal{A}^{\mathrm{T}}P - P\mathcal{A} - 2I_{14} \end{bmatrix} \succeq 0.$$

3.4 Simulation of the interval observer

For a patient without fever, *i.e.* at $37°$C, the parameters of the matrix A have the following constant values [2],:

$$\gamma_1 = 1.96, \gamma_2 = 3.78, \gamma_3 = 2.85, \gamma_4 = 1.76, \gamma_5 = 3.26;$$
$$\mu_1 = 0, \mu_2 = 1.86, \mu_3 = 0, \mu_4 = 0.1, \mu_5 = 0;$$
$$\mu_x = \frac{1}{120}, r = 16, \mu_m = 72.$$

Assume that admissible deviations of these parameters from the nominal values given above are $\sigma\%$, then we can calculate the matrices $\underline{A}$ and $\overline{A}$. The nominal value of healthy RBC recruitment is $\Lambda_0 = \frac{5\times10^6}{120}$ cellsμl^{-1}day^{-1} (the unit of volume is micro-liter (μl) and the unit of time is day) with admissible deviations $\pm 20\%$, *i.e.*

$$0.8\Lambda_0 = \underline{\Lambda} \leq \Lambda(t) \leq \overline{\Lambda} = 1.2\Lambda_0 \ \forall t \geq 0.$$

For simulations we selected:

$$\Lambda(t) = \Lambda_0(1 + 0.2\sin(3t)),$$
$$\beta(t) = 10^{-6}(1 + 0.5\sin(2t))e^{\mathrm{mod}^2(t,2.5+0.5\sin(0.5t))},$$
$$v(t) = V\sin(25t),\ V = 10,$$
$$A(t) = \sin^2(t)\underline{A} + \cos^2(t)\overline{A}.$$

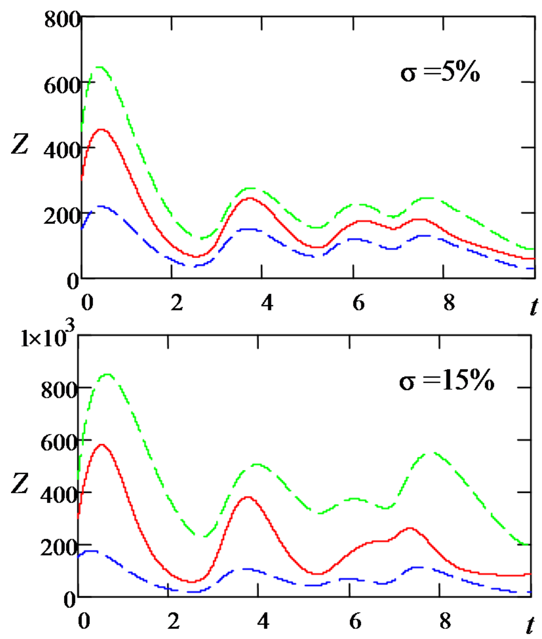

Figure 3.1: The results of interval estimation for sequestered parasites

Let $\underline{z}(0) = \frac{1}{3}\bar{z}(0) = [500\ 100\ 150\ 50\ 50\ 50\ 50]^{\mathrm{T}}$. For differentiator (1.3), $\alpha = 10^3$, $\varrho = 3\alpha$ and $\chi = 0.25\alpha$, then $V' = 30V$ and

$$\underline{L} = \left(1 - \frac{\sigma}{100}\right) [0\ 0\ \gamma_1\ 0\ 0\ 0\ 0]^{\mathrm{T}},$$
$$\overline{L} = \left(1 + \frac{\sigma}{100}\right) [0\ 0\ \gamma_1\ 0\ 0\ 0\ 0]^{\mathrm{T}}$$

have been selected. Assumption 6 holds for these choices of $\overline{L}$ and $\underline{L}$ and all conditions of Theorem 5 are satisfied. The results of interval estimation of sequestered *Plasmodium* $Z(t)$ are shown in Fig. 3.1 for $\sigma = 5$ and $\sigma = 15$. As we can conclude, the dynamics uncertainty σ influences seriously on the estimation accuracy.

3.5 Conclusion

An interval observer is proposed in this chapter in order to estimate the sequestered parasite population from the measured circulating parasites. The efficiency of this technique is shown using the measurements of the circulating parasitaemia $y_1 + y_2$ provided by [2].

Conclusion

First and foremost, interval state estimation for hybrid linear systems has been considered in this report. The goal of the proposed approaches is to take into account the presence of disturbance or uncertain parameters during the synthesis of these interval observers. Two main techniques have been proposed. The first one is based on a static transformation of coordinates, which connects a linear hybrid system with its nonnegative representation when the system is asymptotically stable with a ranged dwell-time. The second technique uses a representation of hybrid system in a nonnegative form. The boundedness of the estimation error (ISS property) and the observer stability can be checked using LMIs. The efficiency of these techniques is shown on examples of computer simulation for two academic systems and a bouncing ball. A future work can focus on nonlinear hybrid systems with parameter uncertainties, and control design based on interval estimates as in [12].

To finish, the design of an interval observer in order to estimate the sequestered parasite population from the measured circulating parasites has been presented in this report. It is assumed that almost all parameters and inputs of the model are uncertain (just intervals of admissible values are given) and the measurements are obtained with a noise. Despite of that the proposed observer demonstrates a reasonable accuracy of interval estimation, which is confirmed by numerical experiments. Further investigations can focus on sampled-time kind of measurements for the estimation of the sequestered parasite population.

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